The Road Ahead: Developing Cutting Edge Strategies for Cancer Treatment

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Cancer Treatment Options

Surgery	→	Remove known tumor masses.
Radiation	→	Kill rapidly dividing tumor cells; kill cells in adjacent tissue.
Chemotherapy	→	Kill rapidly dividing tumor cells.
Hormonal Therapy	→	Inhibit growth and survival of hormone-dependent tumor cells.
Targeted Therapy	→	Specifically inhibit processes required for tumor cell growth.

DeVita, Jr., Hellman, & Rosenberg (Eds.), 2001.

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Targeted Therapies

- Targeted therapies are directed toward specific pathways:
  - Antigen
  - Growth factor
  - Receptor
  - Other molecule
- Targeted therapies moderate, control, or kill cancer cells.

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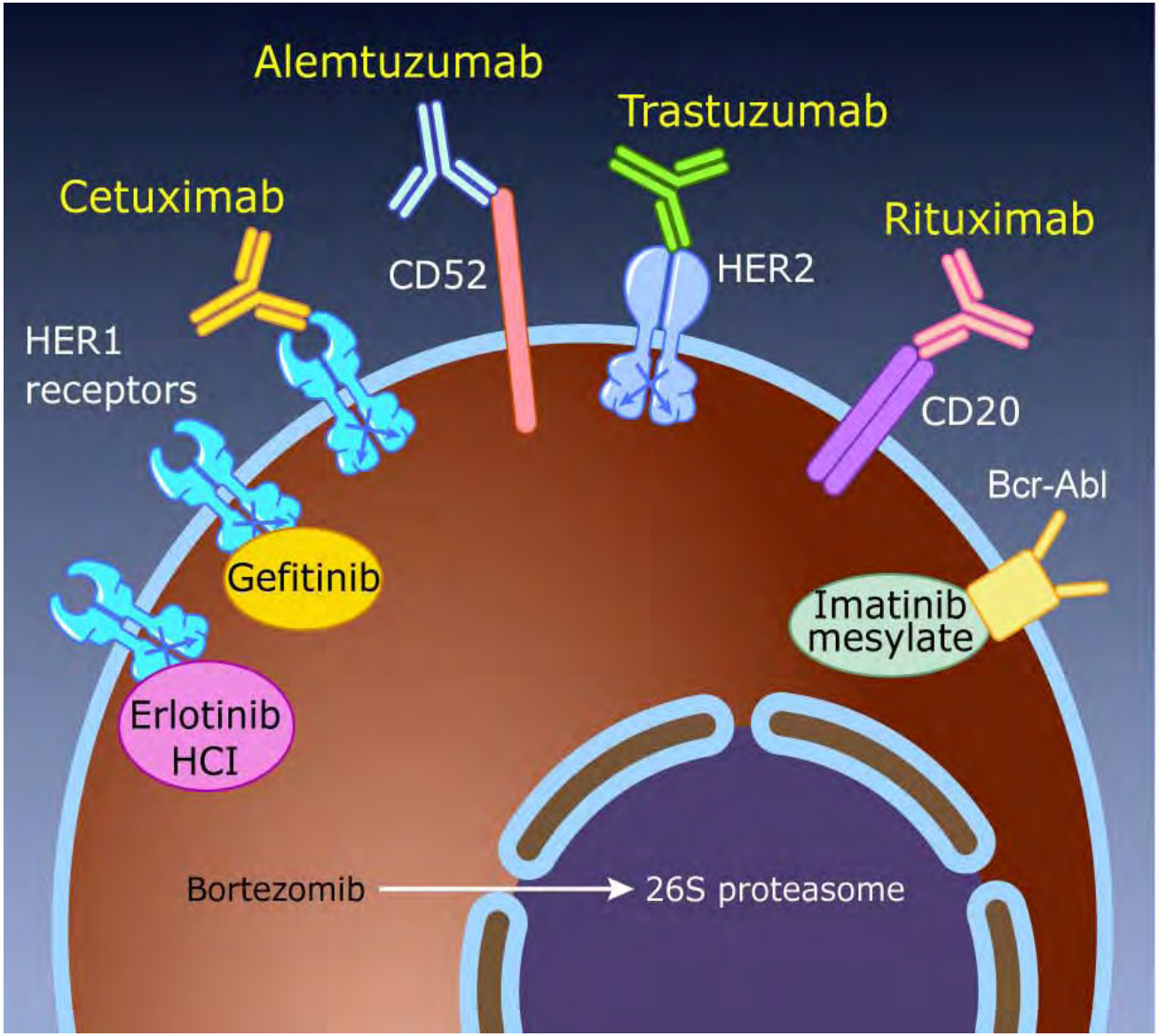
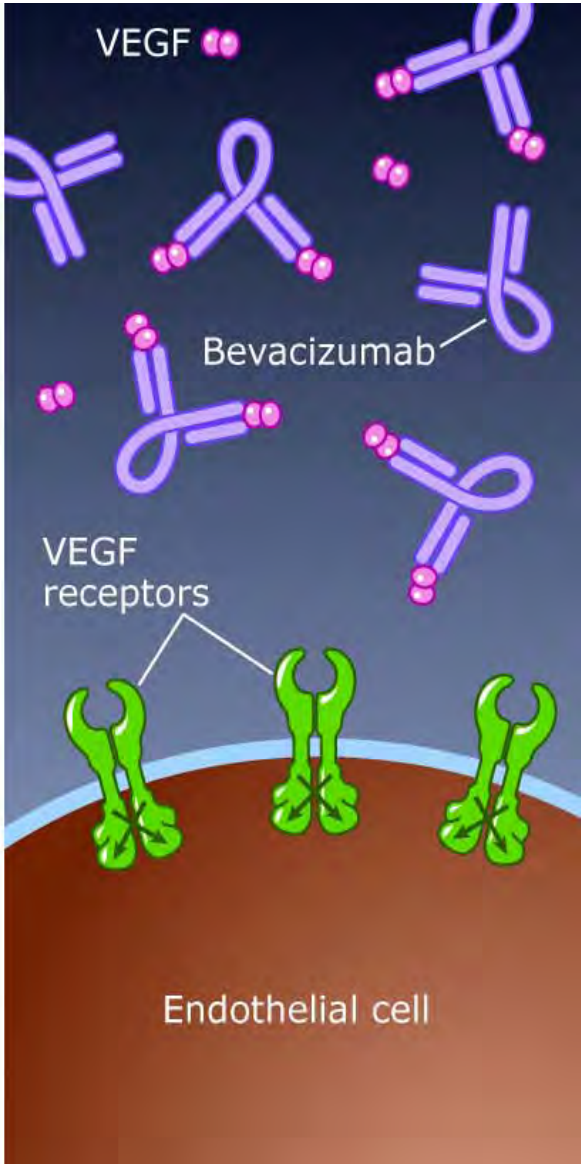
Targeted Therapies





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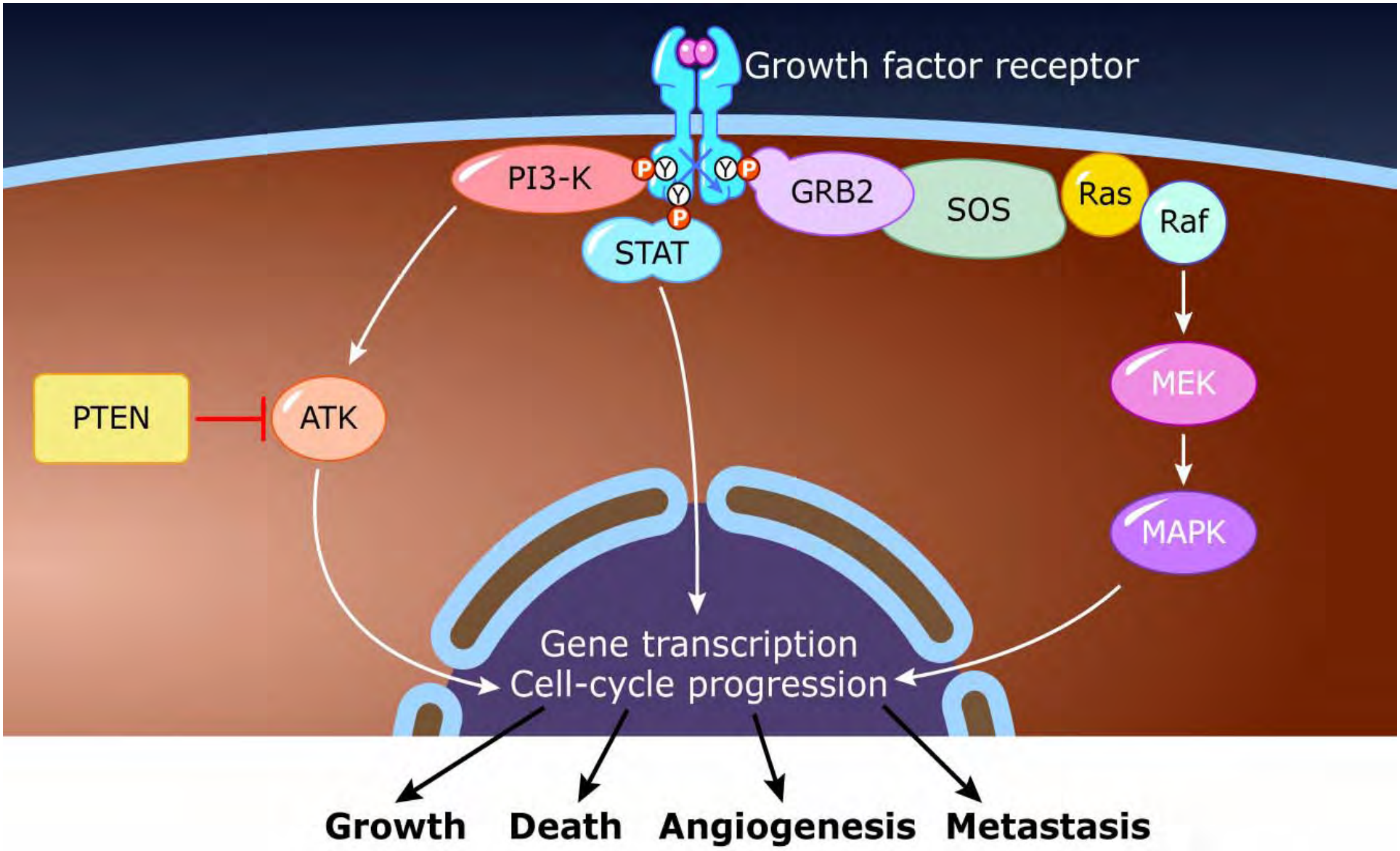
Signal Transduction

- **Signal transduction is the communication process used by regulatory molecules to mediate essential cell processes.**
  - **Essential cell processes:**
    - **Growth**
    - **Differentiation**
    - **Survival**

  Aberrations lead to:

  - **increased proliferation, sustained angiogenesis, tissue invasion and metastases, and apoptosis inhibition**

Epidermal Growth Factor Receptor



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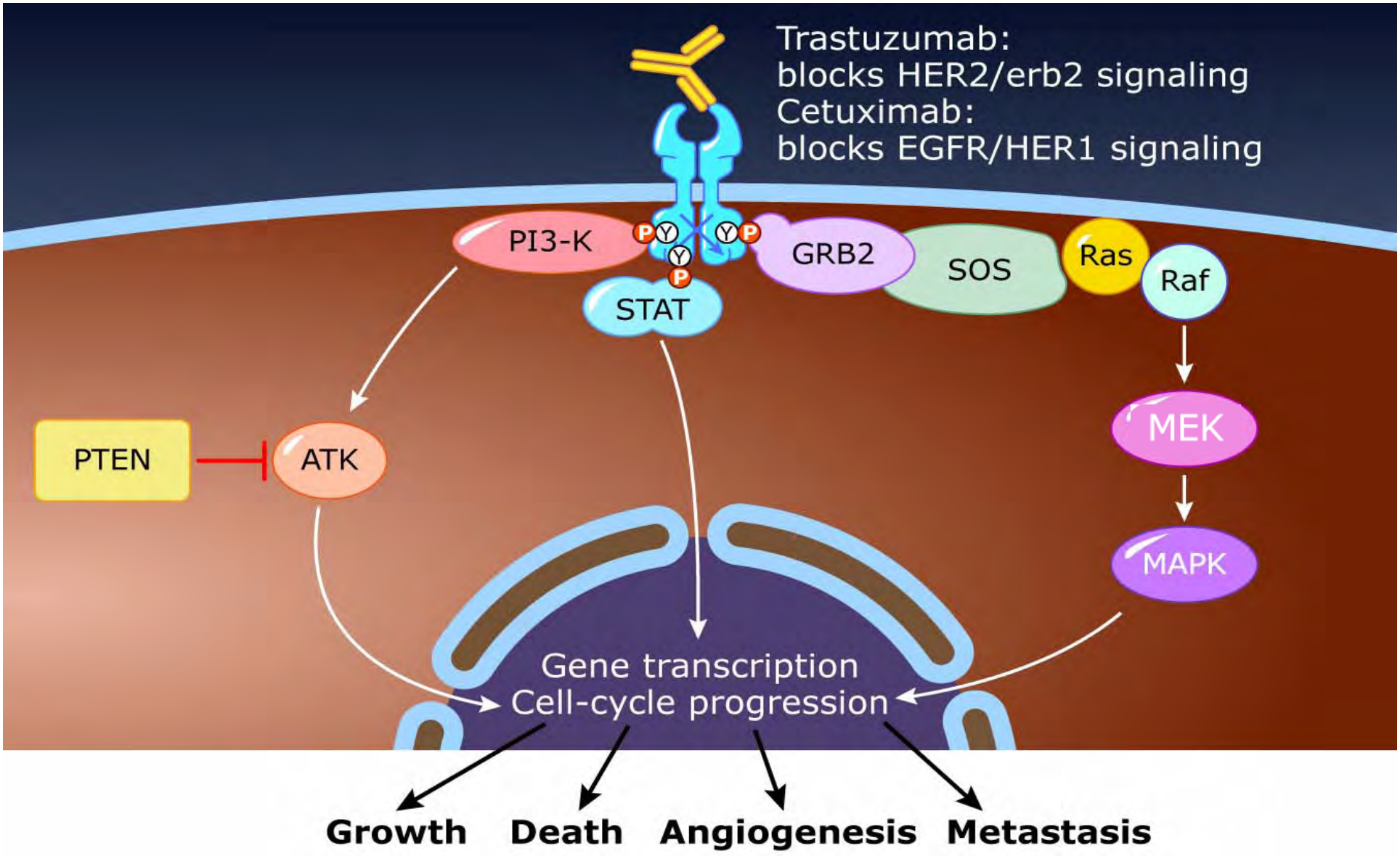
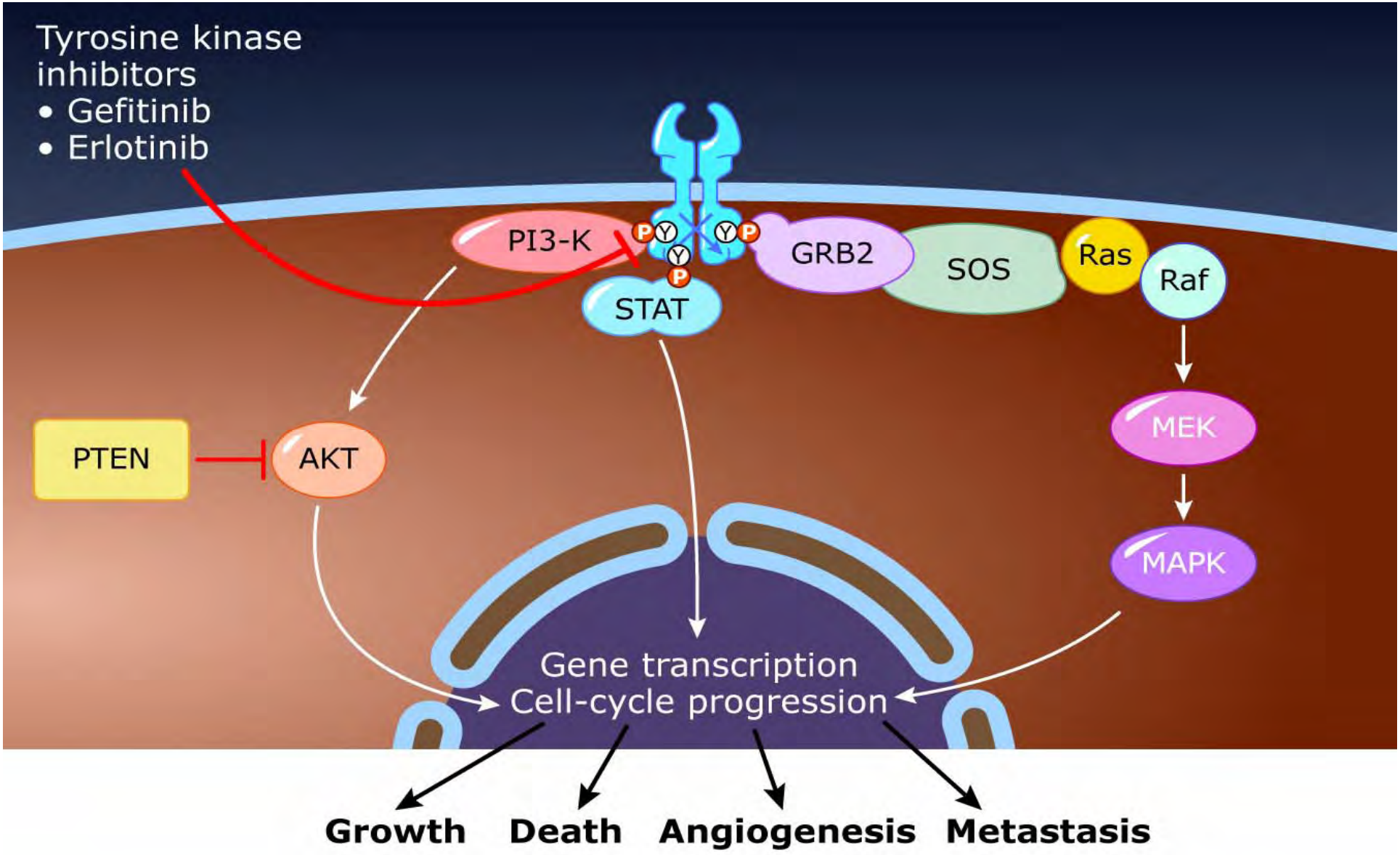
EGFR

- Epidermal growth factor
  - Was discovered in the 1960s by Stanley Cohen
  - Stimulates proliferation of epidermal basal cells
- Growth factor receptors
  - The growth factor receptor was sequenced and cloned in 1984.
  - It plays a role in cell function, growth, and cellular interaction.
- Protein kinases
  - Tyrosine kinases were identified in the 1980s.

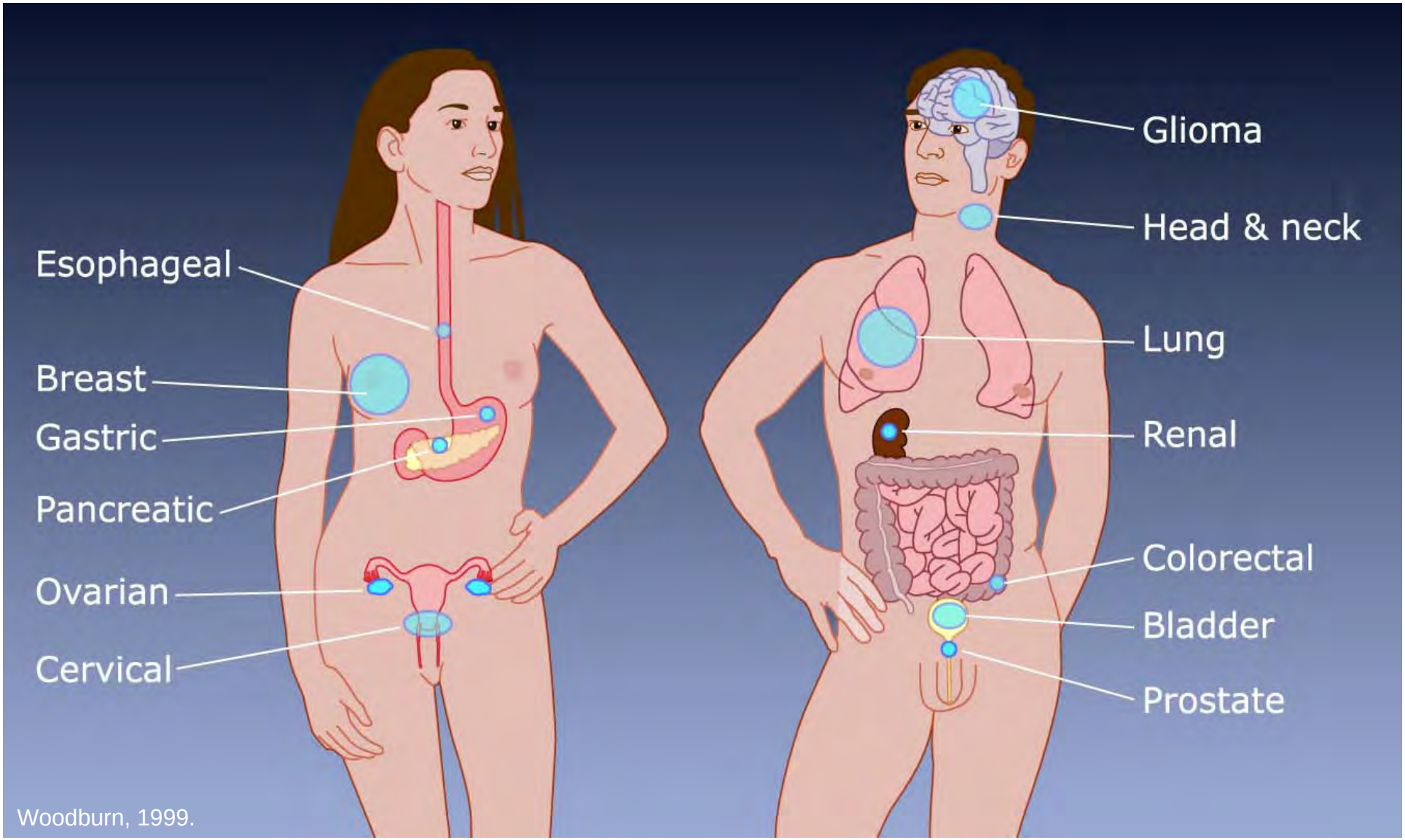
Anti-EGFR Antibodies



Tyrosine Kinase Inhibitors



Tumors With Human Epidermal Growth Factor Receptor Dysregulation



Woodburn, 1999.

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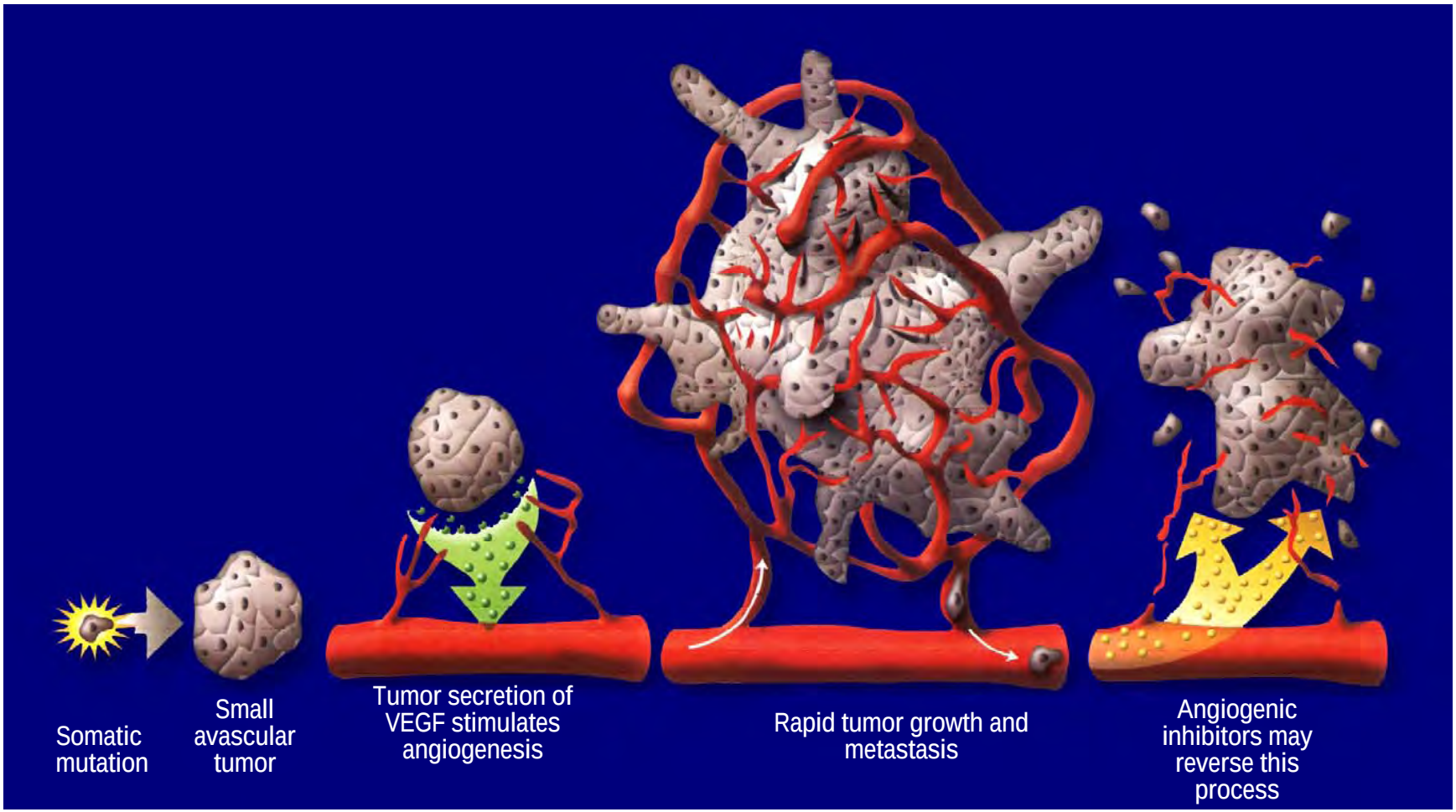
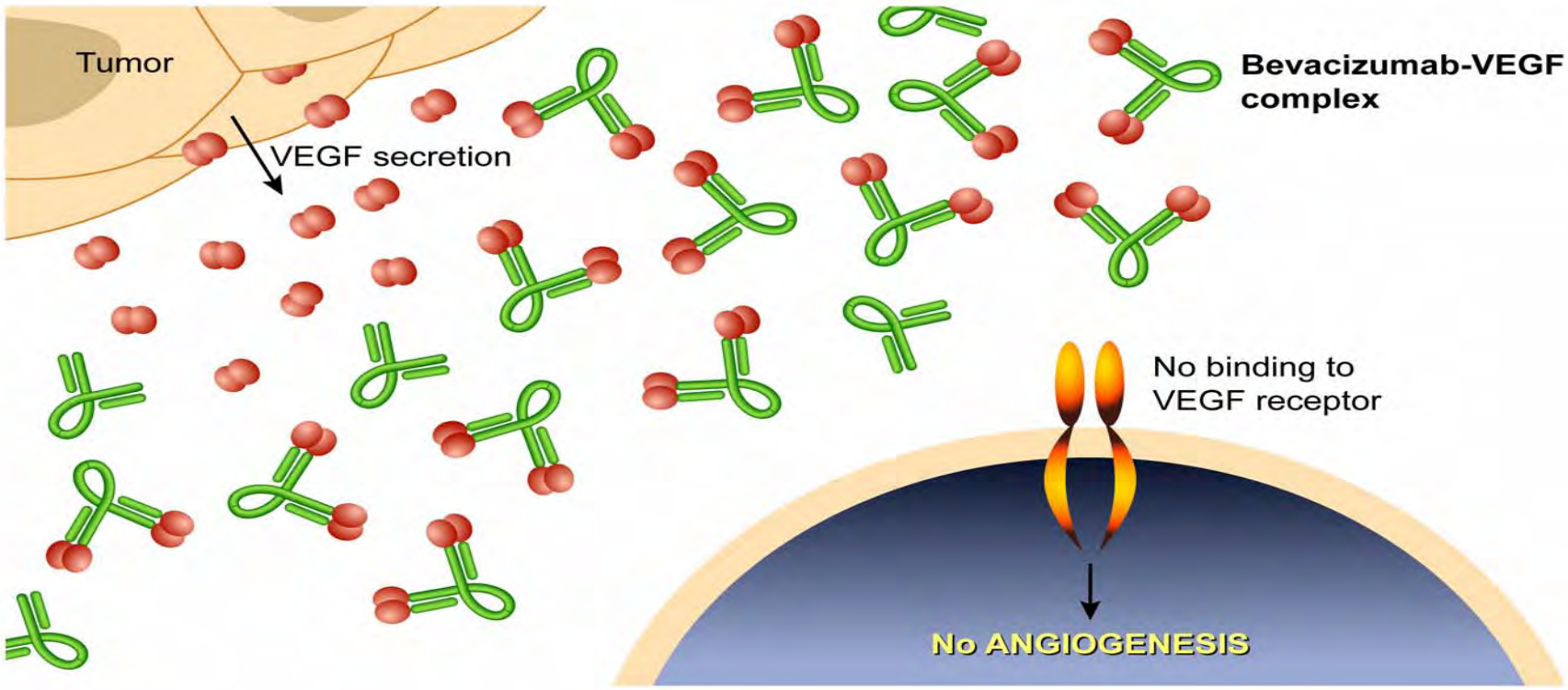
Angiogenesis

- Formation of new blood vessels
- Physiological angiogenesis
  - Embryonic vasculogenesis
  - *de novo* formation from endothelial-cell precursors
  - New vessels form from pre-existing capillaries
- Pathologic angiogenesis
  - Loss of balance between positive and negative controls

Inhibition of VEGF Pathway



Targeting VEGF



FDA approved targeted agents

- 8 monoclonal antibodies
  - Breast cancer
  - Colon cancer
  - Head and neck cancer
  - Non-Hodgkin lymphoma
  - B-cell chronic lymphoctyic leukemia
  - Acute myeloid leukemia

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FDA approved targeted agents

- 6 small molecule agents
  - Chronic myeloid leukemia
  - Gastrointestinal stromal tumors
  - Non-small cell lung cancer
  - Pancreatic cancer
  - Renal cell carcinoma
  - Multiple myeloma

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FDA approved targeted agents

- Single targets
- Multi-targets

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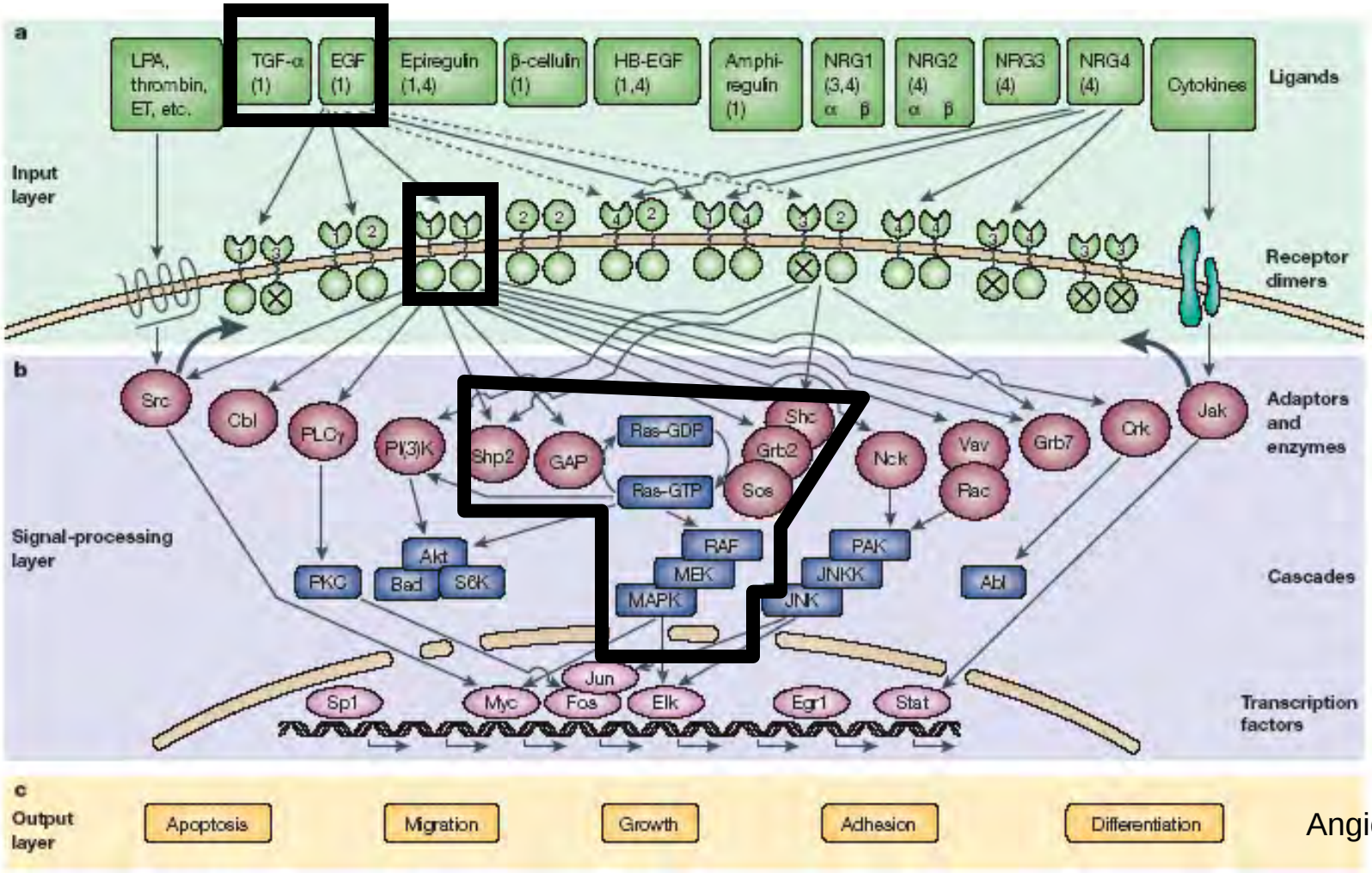
Future Directions with Targeted Therapies

- Combinations with chemotherapy and radiation regimens
- Combinations of targeted agents
- Targeted agents directed toward new growth factors, receptors, pathways
- Targeted agents that can attack multiple growth factors, receptors, pathways

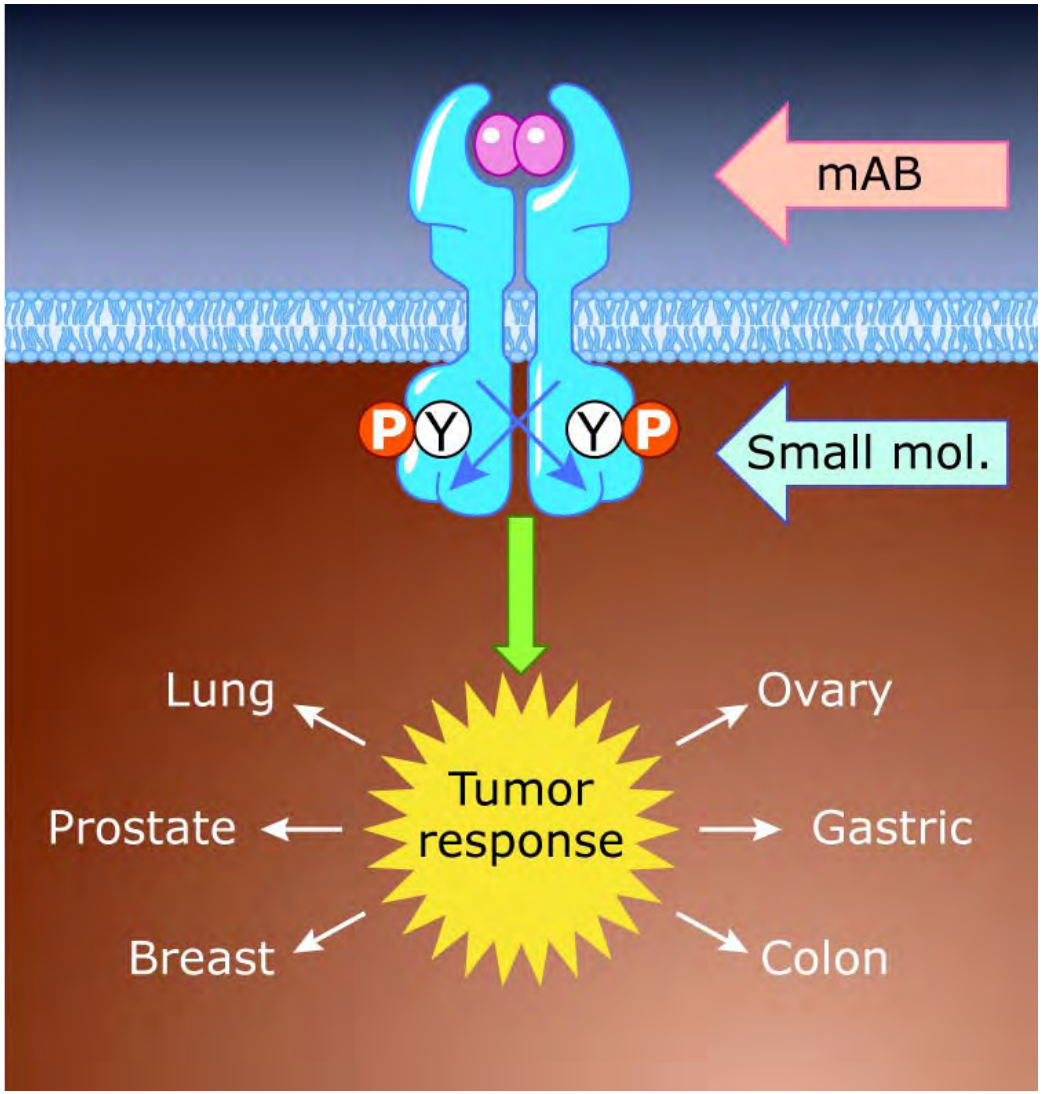
EGFR Signaling



Angiogen

Yarden, Nat Rev Mol Cell Biol 2001;2:127

The Pathway from Concept to Clinical Trials



- The concept:
  - Targeted therapy may have potential with a broad range of malignancies
- Clinical trials:
  - Targeted therapy is well-tolerated.
  - Tumor responses have been seen in several tumor types.
- The promise:
  - Targeted therapies may improve outcomes in the treatment of cancer.

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How do we continue to make progress?

- Correlative studies
  - Tissue collection
  - Profiling studies
  - Genetic studies
- Clinical trials
  - Phase I
  - Phase II
  - Phase III

Hope is the thing
with feathers
that perches in the soul,

And sings the tune
Without the words
and never stops
at all

Emily Dickinson